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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/716,846	11/18/2003	Chaitan Khosla	STAN-258CIP	6797

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EXAMINER

AUDET, MAURY A

ART UNIT	PAPER NUMBER
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1654

DATE MAILED: 09/26/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 10/716,846	<b>Applicant(s)</b> KHOSLA ET AL.	
	<b>Examiner</b> Maury Audet	<b>Art Unit</b> 1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 30 June 2006.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1,3-5 and 11-14 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,3-5 and 11-14 is/are rejected.
- 7) ☒ Claim(s) 1,3-5 and 11-14 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date <u>See cont.</u> | 6) <input type="checkbox"/> Other: _____  |

IDS's: 12/17/03, 02/24/04, 06/04/04, 07/22/04, 02/03/05, 05/05/05, 07/14/06, 07/14/06.

**DETAILED ACTION*****Election/Restrictions***

Applicant's election with traverse of Group I, claims 1, 3-5, and 11-14, as drawn to the elected compound of the invention, {(S)-1-[(3-Bromo-4,5-dihydro-isoxazol-5-ylmethyl)-carbamoyl]-2-phenyl-ethyl}-carbamic acid benzyl ester, and the species method of use for Celiac Sprue, in the reply filed on 06/30/2006, is acknowledged. The traversal is on the ground(s) that the genus formula and expressly claimed compounds, all contain a core comprising an isoxazole moiety. This is not found persuasive because isoxazole (or any moiety containing such), is not a novel compound. (Although these compounds/methods require specific compound database searches to constitute a reasonable search, even a simple term search of patents/publications for "isoxazole" and "Celiac Sprue" or "dermatitis herpetiformis" produced at least 74 references, some or all of which would have to then be reviewed for earlier effective filing dates/teachings relevant to the present claims (e.g. claim 1)/application). Thus, no substantial novel core exists among the genus formula/compound, which would allow for a coextensive search of said compounds in the present methods of use. In other words, any compound comprising an isoxazole moiety (or the distinctly claimed compounds), would have to be separately and individually searched and examined on its own merits to determine its novelty/unobviousness in the present methods. [Absent evidence to the contrary, as noted the restriction requirement, that any prior art references found on any compound bearing an isoxazole moiety for use in the present methods of use, would render obvious any other compound bearing an isoxazole moiety for use in the same present methods of use; should Applicant so choose to prosecute the present application].

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Claims 1, 3-5, and 11-14, are pending and examined on the merits, however, only as drawn to the elected invention, namely a method of treating Celiac Sprue (elected species) using the elected compound of the invention, e.g. a method of treating Celiac Sprue (and/or dermatitis herpetiformis) comprising the elected compound of the invention {(S)-1-[(3-Bromo-4,5-dihydro-isoxazol-5-ylmethyl)-carbamoyl]-2-phenyl-ethyl}-carbamic acid benzyl ester.

The requirement is still deemed proper and is therefore made FINAL.

*Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 3-5, and 11-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Castelhana et al. I (US 4,912,120) or Castelhana et al. II (US 4,929,630) in view of Piper et al. (Biochemistry. 2002 Jan 8;41(1):386-93).

Castelhana et al. I & II both teach the isoxazole moiety compound (elected compound of invention) {(S)-1-[(3-Bromo-4,5-dihydro-isoxazol-5-ylmethyl)-carbamoyl]-2-phenyl-ethyl}-carbamic acid benzyl ester (e.g. associated RN #'s: 115329-49-2, 120245-03-6, 120244-83-9, 148416-83-5), for use as a transglutaminase inhibitor (entire documents, each), orally and in any known formulation at the time (e.g. enteric coated). Although Castelhana et al. I & II teach the use of the compound to mammals suffering from a disease characterized by elevated

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transglutaminase activity, e.g. acne, psoriasis, cataracts, etc.; the references do not expressly include Celiac Sprue in the examples of diseases/disorders within this genus.

Piper et al. expressly teach the high selectivity of human tissue transglutaminase for immunoactive gliadin peptides and that transglutaminase elevation is diagnostic of Celiac Sprue (see e.g. title, abstract, entire document).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to treat the elevated transglutaminase associated disease/disorder Celiac Sprue with {(S)-1-[(3-Bromo-4,5-dihydro-isoxazol-5-ylmethyl)-carbamoyl]-2-phenyl-ethyl}-carbamic acid benzyl ester in either Castelhana et al. I & II, because Piper et al. advantageously teach that elevated transglutaminase is diagnostic of Celiac Sprue (similar to other elevated transglutaminase associated diseases/disorders) and Castelhana et al. I & II advantageously teach that {(S)-1-[(3-Bromo-4,5-dihydro-isoxazol-5-ylmethyl)-carbamoyl]-2-phenyl-ethyl}-carbamic acid benzyl ester is a transglutaminase inhibitor. An autoimmune disease/disorder practitioner would have been motivated to select the transglutaminase inhibitor {(S)-1-[(3-Bromo-4,5-dihydro-isoxazol-5-ylmethyl)-carbamoyl]-2-phenyl-ethyl}-carbamic acid benzyl ester in the treatment of a patient suffering from Celiac Sprue, with a reasonable expectation of success, based on the advised therapeutic effect of this compound for use in other elevated transglutaminase associated diseases/disorders (Castelhana et al. I & II), of which Celiac Sprue was discovered to share this same pathophysiologic pathway (Piper et al.).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at

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the time the invention was made, as evidenced by the reference, especially in the absence of evidence to the contrary.

### ***Claim Objections***

Claims 1, 3-5, and 11-14 are objected to because of the following informalities: the claims are drawn to non-elected inventions. In response to the present Office Action, Applicant is asked to amend the claims to be drawn to the elected invention (e.g. 1, 3-5, and 11-14). Appropriate correction is required.

### ***Specification***

On page 4, 1<sup>st</sup> paragraph, the sentence is missing a period (“.”).

### ***Conclusion***

No claims are allowed.

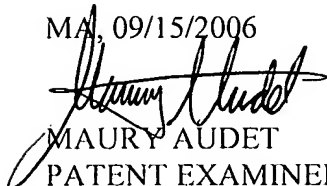
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maury Audet whose telephone number is 571-272-0960. The examiner can normally be reached on M-Th. 7AM-5:30PM (10 Hrs.).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecelia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MA, 09/15/2006

  
MAURY AUDET  
PATENT EXAMINER  
ART UNIT 1654